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December 22, 2021

VIA ECF
Honorable Julian Xavier Neals, U.S.D.J.
U.S. District Court for the District of New Jersey
Martin Luther King Jr. Building & U.S. Courthouse
50 Walnut Street
Newark, New Jersey 07102

Re: *Corcept Therapeutics, Inc. v. Teva Pharmaceuticals USA, Inc.*
Civil Action No.: 2:18-cv-3632-JXN-LDW (Consolidated)

Dear Judge Neals:

This firm, together with Sterne, Kessler, Goldstein & Fox, P.L.L.C., represents Teva in the above-captioned matter. We write to respectfully renew Teva's August 24, 2021 letter request (Dkt 223) that argument be scheduled on the parties' pending cross-motions for summary judgment regarding infringement of the '214 patent, *see* Dkt 197; Dkt 203, and/or a date be set for trial at the Court's earliest convenience, as well as to provide the Court with an update concerning the '214 patent.

As previously noted, this is a Hatch-Waxman patent-infringement case that has been pending for nearly four years and stands ready for trial on the two remaining patents-in-suit (the '214 patent and the '216 patent). The statutorily mandated 30-month stay of FDA approval of Teva's generic version of Corcept's drug Korlym (mifepristone), which was triggered when Corcept filed its complaint in March 2018, expired eighteen months ago, in August 2020. Teva has had final FDA approval to market its generic mifepristone product since August of 2020 and therefore has the ability to bring its lower-cost alternative to patients suffering from Cushing's syndrome. Thus, there is a strong interest on the part of Teva and the public in concluding this case as soon as possible. While Corcept argued in its August 27th letter (Dkt. 225) that there is nothing prohibiting Teva from launching its product while the case is pending, Corcept does not commit to not burdening the Court or Teva with time-consuming and costly motion practice for injunctive relief if Teva were to launch prior to the Court's decision in this case. Thus, Corcept's arguments ring hollow.

The parties' summary judgment motions concerning infringement of the '214 patent are fully briefed and pending before the Court, and Teva would welcome the opportunity for a hearing on those motions should Your Honor believe argument would be helpful to the Court. Dkt 197-199; Dkt 202-203; Dkt 209-211; Dkt 213. The infringement issues concerning the '214 patent are now the only issues remaining on that patent as the Federal Circuit recently affirmed the Patent Trial and Appeal Board decision upholding the patentability of the '214 patent. A copy of the Federal Circuit's slip opinion is enclosed for the Court's convenience. Of course, if the Court would prefer to reserve on the motions and proceed to trial, Teva respectfully renews its

request that the Court calendar this case for a three-day bench trial at the Court's earliest convenience.

Teva greatly appreciates the Court's consideration of this submission and is available should Your Honor have any questions or wish to hear from the parties concerning Teva's request.

Respectfully submitted,

s/Liza M. Walsh

Liza M. Walsh

cc: All Counsel of Record (via ECF and Email)

United States Court of Appeals for the Federal Circuit

TEVA PHARMACEUTICALS USA, INC.,
Appellant

v.

CORCEPT THERAPEUTICS, INC.,
Appellee

2021-1360

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. PGR2019-00048.

Decided: December 7, 2021

JOHN CHRISTOPHER ROZENDAAL, Sterne Kessler Goldstein & Fox, PLLC, Washington, DC, argued for appellant. Also represented by UMA EVERETT, WILLIAM MILLIKEN, OLGA A. PARTINGTON, DEBORAH STERLING.

ERIC C. STOPS, Quinn Emanuel Urquhart & Sullivan, LLP, New York, NY, argued for appellee. Also represented by WILLIAM ADAMS, FRANK CHARLES CALVOSA, FRANCIS DOMINIC CERRITO, DANIEL C. WIESNER.

Before MOORE, *Chief Judge*, NEWMAN and REYNA, *Circuit Judges*.

MOORE, *Chief Judge*.

In a final-written decision, the Patent Trial and Appeal Board held that Teva Pharmaceuticals USA had failed to show claims 1–13 of U.S. Patent No. 10,195,214 would have been obvious. *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, PGR2019-00048, 2020 WL 6809812 (P.T.A.B. Nov. 18, 2020) (*Final Decision*). Teva appeals, arguing the Board misapplied our obviousness law.[1] For the following reasons, we affirm.

I

A

In the 1980s, mifepristone was developed as an antiprogestin. *See* J.A. 1009. But researchers soon realized mifepristone functions as a glucocorticoid reception antagonist, meaning it likely inhibits the effect of cortisol on tissues by competing with cortisol for receptor binding sites. *See* J.A. 870, 1037. As a result, they suggested using mifepristone to treat Cushing's syndrome, a disease caused by excessive levels of cortisol. J.A. 1034–38.

More than 20 years later, Corcept Therapeutics, Inc., initiated the first major clinical trial of mifepristone in patients with Cushing's syndrome. J.A. 1252. Over a 24-week period, 50 participants were given one daily dose of mifepristone, starting at a dosage of 300 mg per day and possibly increasing to a maximum dosage of 1200 mg per day. J.A. 1259. That administration "produced significant clinical and metabolic improvement in patients with [Cushing's syndrome] with an acceptable risk-benefit

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[1] Teva also argues that, under the correct standards, the challenged claims would have been obvious. Because we discern no legal error, we need not reach that argument.

profile during 6 months of treatment." J.A. 1259; *accord* J.A. 1259–61.

Based on its successful study, Corcept filed a New Drug Application (NDA) for Korlym, a 300 mg mifepristone tablet. It sought approval for the administration of Korlym to control "hyperglycemia secondary to hypercortisolism" in certain patients with Cushing's syndrome. J.A. 982. The U.S. Food and Drug Administration approved Corcept's application, but imposed a few postmarketing requirements under 21 U.S.C. § 355(o)(3). One requirement was to conduct "[a] drug-drug interaction clinical trial to determine a quantitative estimate of the change in exposure of mifepristone following co-administration of ketoconazole (a strong CYP3A4 inhibitor)." J.A. 984.

To summarize the drug-drug interaction study requirement, the FDA provided Corcept with an Office of Clinical Pharmacology memorandum. *See* J.A. 865–900 (hereinafter, Lee). That memorandum explained that "[t]he degree of change in exposure of mifepristone when co-administered with strong CYP3A inhibitors is unknown . . . ." J.A. 865. Thus, Lee noted that co-administration "may present a safety risk" and that, without a drug-drug interaction study, a "lack of accurate knowledge" may "deprive the patients on strong inhibitors [of] the use of [m]ifepristone." *Id.* Lee also noted that, "[b]ased on the results of this study, the effect of moderate CYP3A inhibitors on mifepristone pharmacokinetics may need to be addressed." J.A. 866.

In approving Corcept's NDA, the FDA also approved the prescribing information for Korlym contained in its label. J.A. 839–49. The FDA-approved Korlym label "recommended [a] starting dose [of] 300 mg once daily" and allowed for increasing the dosage "in 300 mg increments to a maximum of 1200 mg once daily" based on clinical assessments. J.A. 839. In addition to those conditions, the Korlym label warned against using mifepristone "with strong

CYP3A inhibitors" and limited the "mifepristone dose to 300 mg per day when used with strong CYP3A inhibitors." J.A. 839.

B

Corcept conducted the drug-drug interaction study described in Lee, collecting data on co-administration of mifepristone with a strong CYP3A inhibitor. Based on that data, Corcept sought and received the '214 patent. The '214 patent relates to methods of treating Cushing's syndrome by co-administering mifepristone and a strong CYP3A inhibitor. Claim 1 is representative for purposes of this appeal:

> A method of treating Cushing's syndrome in a patient who is taking an original once-daily dose of 1200 mg or 900 mg per day of mifepristone, comprising the steps of:
>
> > reducing the original once-daily dose to an adjusted once-daily dose of 600 mg mifepristone,
> >
> > administering the adjusted once-daily dose of 600 mg mifepristone and a strong CYP3A inhibitor to the patient,
> >
> > wherein said strong CYP3A inhibitor is selected from the group consisting of ketoconazole, itraconazole, nefazodone, ritonavir, nelfmavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir, and voriconazole.

After Corcept asserted the '214 patent against Teva in district court, Teva sought post-grant review of claims 1–13. Teva argued those claims would have been obvious in light of Korlym's label and Lee, optionally in combination

with FDA guidance on drug-drug interaction studies. In support of its petition, Teva provided a declaration from Dr. David J. Greenblatt. Most relevant here, Dr. Greenblatt opined that, based on the Korlym label and Lee, "it was reasonably likely that 600 mg [per day of mifepristone] would be well tolerated and therapeutically effective when co-administered with a strong CYP3A inhibitor." J.A. 681. The Board instituted review on all asserted grounds.

In its final-written decision, the Board held Teva had failed to prove claims 1–13 would have been obvious to a skilled artisan. It first construed the claims to require safe administration of mifepristone. *Final Decision* at *7–9. Then, the Board found Teva failed to show that a skilled artisan would have had a reasonable expectation of success for safe co-administration of more than 300 mg of mifepristone with a strong CYP3A inhibitor. *Id.* at *10–22. In doing so, it discredited the above-quoted statement from Dr. Greenblatt, finding it inconsistent with his later testimony and other evidence in the record. Teva appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(4).

II

Teva faults the Board for, in its view, committing two legal errors. First, it claims the Board required precise predictability, rather than a reasonable expectation of success, in achieving the claimed invention. That is, Teva argues the Board improperly required it "to show an expectation that the *specific* dose recited in the claims would have been safe." Appellant's Br. at 41. Second, Teva claims the Board ought to have applied our prior-art-range precedents. In Teva's view, the Board committed legal error when it found Teva had failed to prove the general working conditions disclosed in the prior art encompassed the claimed invention. We do not agree.

A

We start by addressing Teva's reasonable-expectation-of-success argument. "The presence or absence of a reasonable expectation of success is . . . a question of fact," which we review for substantial evidence. *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1366 (Fed. Cir. 2016). Whether the Board applied the correct standard in assessing reasonable expectation of success, however, is a question of law that we review de novo. *See Endo Pharms. Inc. v. Actavis LLC*, 922 F.3d 1365, 1377–78 (Fed. Cir. 2019).

The Board did not err by requiring Teva to show a reasonable expectation of success for a specific mifepristone dosage. The reasonable-expectation-of-success analysis must be tied to the scope of the claimed invention. *See Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 966 (Fed. Cir. 2014) ("[F]ailure to consider the appropriate scope of the . . . claimed invention in evaluating the reasonable expectation of success . . . constitutes a legal error . . . ."); *see also Intelligent Bio-Sys., Inc.*, 821 F.3d at 1367. Here, claim 1 of the '214 patent requires safe administration of a specific amount of mifepristone, 600 mg per day. *See Final Decision* at *7–9 (construing claims to require safe administration, rather than just administration). Thus, the Board was required to frame its reasonable-expectation-of-success analysis around that specific dosage of mifepristone. To be clear, this does not mean Teva was required to prove a skilled artisan would have precisely predicted safe co-administration of 600 mg of mifepristone. Absolute predictability is not required. *See, e.g.*, *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007). But Teva was required to prove a reasonable expectation of success in achieving the specific invention claimed, a 600 mg dosage.

Applying that standard, the Board found Teva had failed to prove a reasonable expectation of success. It found that Teva had "not established . . . that [a skilled artisan]

would reasonably have expected co-administration of more than 300 mg of mifepristone with a strong CYP3A inhibitor to be safe for the treatment of Cushing's syndrome or related symptoms in patients." *Final Decision* at *22; *see also id.* at *10–22. It went even further, finding "the evidence support[ed] that [a skilled artisan] would have had *no expectation* as to whether co-administering dosages of mifepristone above the 300 mg/day threshold set forth in the Korlym label would be successful." *Id.* at *20 (emphasis added). Because there was no expectation of success for any dosage over 300 mg per day, there was no expectation of success for the specific 600 mg per day dosage. *See id.* at *14 (finding no expectation of success for 600 mg per day dosage). Under our precedent, those findings were dispositive. *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. DE C.V.*, 865 F.3d 1348, 1356 (Fed. Cir. 2017) (holding the reasonable-expectation-of-success requirement is not satisfied when the skilled artisan would have had no expectation of success). Nothing about this analysis required precise predictability, only a reasonable expectation of success tied to the claimed invention.

The Board's treatment of Dr. Greenblatt's testimony is similar. Before institution, Dr. Greenblatt opined that "it was *reasonably likely* that 600 mg [per day of mifepristone] would be well tolerated and therapeutically effective when co-administered with a strong CYP3A inhibitor." J.A. 681 (emphasis added). But the Board discredited that opinion based on Dr. Greenblatt's later, inconsistent testimony that "unequivocally" stated a skilled artisan "would have *no expectation* as to whether the co-administration of 600 mg of mifepristone with ketoconazole would be safe." *Final Decision* at *11 (emphasis added) (discussing testimony at J.A. 5493–94). The Board found the later testimony, unlike Dr. Greenblatt's pre-institution testimony, was consistent with his other deposition testimony, *id.* at *12 (discussing J.A. 5511); his post-deposition declaration, *id.* (discussing J.A. 3096–97); and other evidence in the record, *id.* at *14

(citing J.A. 1164–66 (Dr. Greenblatt article), 3111 (Dr. Dobbs declaration), 3433 (Dr. Guengerich testimony)). The Board then considered and rejected Teva's attempt to square Dr. Greenblatt's declaration with his deposition testimony. *Id.* at *13–14. Put simply, the Board found Dr. Greenblatt's testimony supported a finding of no expectation of success in achieving the claimed invention, not that Dr. Greenblatt had failed to show the specific claimed dosage was absolutely predictable in advance.[2]

In sum, we see no reversible error in the Board's reasonable-expectation-of-success analysis. The Board applied the correct standard, requiring only a reasonable expectation of success and tying its analysis to the scope of the claimed invention.

B

We next address the applicability of our prior-art-range cases—i.e., the cases in which a claimed range of values overlap the ranges disclosed in the prior art. The Board declined to apply those cases because it found Teva had failed to prove the general working conditions disclosed in the prior art encompass the claimed invention. The scope and content of the prior art is a question of fact, reviewed for substantial evidence. *SIPCO, LLC v. Emerson Elec. Co.*, 980 F.3d 865, 870 (Fed. Cir. 2020).

"For decades, this court and its predecessor have recognized that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) (quotation marks omitted). "A more specific application of this general principle is that a

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[2] To the extent Teva challenges the Board's credibility findings, *see* Appellant's Br. at 39–40, they are supported by substantial evidence.

prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *Id.* (quotation marks and alterations omitted). But overlap is not strictly necessary for a conclusion of obviousness: "obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003); *accord In re Brandt*, 886 F.3d 1171, 1177 (Fed. Cir. 2018); *Valeant Pharms. Int'l, Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 32 (Fed. Cir. 2020).

Substantial evidence supports the Board's finding that the general working conditions disclosed in the prior art did not encompass the claimed invention, i.e., there was no overlap in ranges. In the Board's view, "the evidence of record support[ed] that the general working conditions limited co-administration of mifepristone with a strong CYP3A inhibitor to just 300 mg/day." *Final Decision* at *21. Rephrased, the prior art capped the range of co-administration dosages at 300 mg per day. For support, the Board cited the Korlym label, *id.*, which cautioned that "[m]ifepristone should be used in combination with strong CYP3A inhibitors only when necessary, and in such cases the dose should be limited to 300 mg per day." J.A. 844. And it also noted how industry publications echoed this limitation. *Final Decision* at *21 (citing J.A. 1279–80 ("[T]he dose of mifepristone should not exceed 300 mg/day if used in combination with ketoconazole."), 4164 (For co-administration with ketoconazole, "the maximum daily dose of mifepristone should be 300 mg.")). The Board's finding that the prior art ranges do not overlap with the claimed range is supported by substantial evidence.

And the Board's reasonable-expectation-of-success finding, which we have already upheld, forecloses Teva's reliance on monotherapy doses above 300 mg per day. Teva claims those monotherapy dosages create an overlap with the claimed range. But monotherapy dosages alone cannot

create an overlap with the claimed range, which is limited to co-administering mifepristone with a strong CYP3A inhibitor. Thus, the only remaining question is whether a skilled artisan would have expected monotherapy and co-administration dosages to behave similarly. As the Board found, a skilled artisan would have had no such expectation. And we have already upheld that finding as supported by substantial evidence.

III

Teva claims this is an "uncommonly clear-cut obviousness case." Appellant's Br. at 37. It describes the prior art as "disclos[ing] the problem, . . . the solution, . . . and the way to find the solution." *Id.* In doing so, it ignores the reasonable-expectation-of-success requirement. At best, the prior art directed a skilled artisan to try combining the Korlym Label, Lee, and the FDA guidance. But without showing a reasonable expectation of success, Teva did not prove obviousness. Since the Board applied the appropriate legal standards in finding no expectation of success and its fact findings are supported by substantial evidence, we affirm.

AFFIRMED